REMARKS

Upon entry of the amendment set forth in Applicants' April 28, 2006 reply, claims 1, 18, 21, and 24 are pending. In addition to the arguments set forth in the April 28th reply, Applicants address the 35 U.S.C. § 112, first paragraph rejection set forth in the final Office Action, as applied to the present claims, as follows.

As an initial matter, Applicants would like to thank Examiner Sisson for the helpful personal interview conducted with Applicants' representative James DeCamp on November 14, 2006.

Claim Amendments

Claims 1 and 18 have been amended to recite *human or murine* granulocyte colony stimulating factor receptors and claim 1 has been amended to recite a *human* estrogen receptor. As noted below, Applicants submit that, as of the priority date of the present application, the sequences of the human and murine granulocyte colony stimulating factor receptors and of the human estrogen receptor were known. In addition, Applicants note that the specification, at page 2, lines 18-21, of the English language translation, describes a fusion protein between "the estrogen receptor and c-Abl tyrosine kinase" and cites Jackson et al. (EMBO J. 12:2809-2819, 1993; "Jackson;" copy enclosed as Exhibit E). Jackson describes a fusion protein containing the hormone-binding domain of the human estrogen receptor (see, e.g., top of the right column on page 2818). Applicants submit that recitation in the specification of "*the* estrogen receptor" therefore refers to the human

estrogen receptor.

Claims 1, 21, and 24 have been amended to recite that amino acid residues 5 (Glu) through 195 (Leu) and 725 through 756 relate to the wild-type *murine* granulocyte colony stimulating factor (G-CSF) receptor. Applicants submit that in view of the description of the sequence of the murine G-CSF receptor sequence in Fukunaga et al. (Cell 61:341-350, 1990; copy enclosed as Exhibit A) one skilled in the art would have recognized that the amino acid residues recited in the claim refer to the wild-type murine sequence. The present amendment contains no new matter.

The present amendments have been made solely to expedite prosecution and Applicants reserve the right to pursue canceled subject matter in this or in a continuing application.

Rejection under 35 U.S.C. § 112, First Paragraph

In the Advisory Action mailed on November 24, 2006, the Office asserts:

> The disclosure does not recite any SEQ ID NO. and the claims are drafted in terms of a compound's functionality, with no recitation of structure-function relationship.

Applicants submit that this basis for rejection may be withdrawn.

The G-CSF Receptor

Turning first to the sequence of the G-CSF receptor deficient in amino acid residues 5 (Glu) through 195 (Leu) of wild-type murine G-CSF receptor, or a G-CSF

receptor deficient in amino acid residues 5 (Glu) through 195 (Leu) and amino acid residues 725 through 756 of wild-type murine G-CSF receptor Applicants submit that there can be no question that the specification as filed provides adequate written description for these sequences. For example, at page 9, lines 16-20, the specification teaches construction of a fusion protein that is deficient in the 5th residue, Glu, through the 195th residue, Leu, of the murine granulocyte colony stimulating factor receptor ("GCRΔ(5-195)/ER"). Further, for example, at page 9, lines 21-24, the specification describes a fusion protein that, in addition to lacking residues 5-195, lacks residues 725-756 of the murine G-CSF receptor ("GCRΔ(5-195, 725-756)/ER"). Moreover, for instance, in Example 6, Applicants teach that such fusion proteins can impart proliferation activity to a blood cell. Applicants submit that these sequences are free of the present rejection under 35 U.S.C. § 112, first paragraph.

The sequence of the human or murine G-CSF receptor recited in claim 1 also finds adequate written description in the specification as filed. In Example 1, Applicants describe constructing a chimeric protein including "the entire G-CSF receptor and the ligand (estrogen)-binding domain of the estrogen receptor ["GCRER"]" (see e.g., page 9, lines 12-14). As such, a fusion protein including a G-CSF receptor is described in the specification as filed. Applicants submit that in view of Applicants' teachings in the specification of fusion proteins containing G-CSF receptor sequences and the knowledge in the art at the time the application was filed, the skilled artisan would recognize a human or murine G-CSF receptor sequence.

In further support of this assertion, Applicants direct the Office's attention to the enclosed Declaration by Dr. Yasuji Ueda, a co-inventor of the presently claimed invention. Here Dr. Ueda states (paragraph 2):

> G-CSF receptors are a class of proteins that were extraordinarily well characterized at the time the application was filed. The structural features, including the Immunoglobulin-like domain, the cytokine receptor homologous domain, the three fibronectin type III domains, and the intracellular domain, defining this class of receptors were also known. For instance, Fukunaga et al. (Cell 61:341-350, 1990; copy enclosed as Exhibit A) describes the murine G-CSF receptor sequence and notes that the sequence is highly homologous to that of the human G-CSF receptor. Larsen et al. (J. Exp. Med. 172:1559-1570, 1990; copy enclosed as Exbibit B) describes the human G-CSF receptor sequence. In addition, Fukunaga et al. (EMBO J.:10:2855-2865, 1991; copy enclosed as Exhibit C) describes functional domains of human and mouse G-CSF receptors. In view of the knowledge in the art at the time the application was filed, a skilled artisan would readily recognize a G-CSF receptor sequence.

Furthermore, Applicants submit that known sequences need not be included in the specification to meet the written description requirement of 35 U.S.C. § 112, first paragraph. As noted in Applicants' April 28, 2006 reply, the Federal Circuit has indicated that § 112 does not impose a *per se* rule requiring recitation in the specification of the nucleotide sequence of claimed DNA, when that sequence is already known in the field. *Capon v. Eshhar,* 418 F.3d 1349, 76 U.S.P.Q. 1078 (Fed. Cir. 2005). The Federal Circuit, in reversing the Board's conclusion that the written description requirement necessitated a listing of the specific nucleotide sequences of the claimed DNA, stated:

> The chimeric genes here at issue are prepared from known DNA sequences of known function. The Board's requirement that these sequences must be analyzed and reported in the specification does not add descriptive substance. The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the

> structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes. (Emphasis added.)

Capon, 418 F.3d at 1358.

In addition, in *Falkner v. Inglis*, 448 F.3d 1357, 79 U.S.P.Q.2d 1001 (Fed. Cir. 2006) the Federal Circuit stated:

> [W]e hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences ... satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences. (Emphasis added.)

Falkner, 79 U.S.P.Q.2d at 1008.

In the present case, human and murine G-CSF receptor sequences were known at the time the application was filed. As stated by the Federal Circuit, these sequences need not be recited in the specification to meet the written description requirement.

Finally, for instance, in Examples 2 and 6, the specification describes fusion proteins containing G-CSF receptor sequences that impart proliferation activity to a blood cell. Thus, Applicants' specification also describes that the presently claimed fusion proteins have the function required by the claims.

For all the above reasons, Applicants submit that the human and murine G-CSF receptor sequences recited in the present claims meet the written description requirement of 35 U.S.C. § 112, first paragraph. This basis for the written description rejection should be withdrawn.

The Estrogen Receptor

The estrogen-binding domain of the human estrogen receptor is also adequately described in Applicants' specification as filed. Applicants note that, for instance, in Example 1 the specification describes constructing a chimeric protein including "the entire G-CSF receptor and the ligand (estrogen)-binding domain of the estrogen receptor ["GCRER"]" (see e.g., page 9, lines 12-14). As such, a fusion protein having a first polypeptide including an estrogen-binding domain of the estrogen receptor and the second polypeptide including a G-CSF receptor is described in the specification as filed.

The specification as filed also describes fusion proteins having a first polypeptide including an estrogen-binding domain of the estrogen receptor and either a G-CSF receptor deficient in amino acid residues 5 (Glu) through 195 (Leu) of wild-type murine granulocyte colony stimulating factor receptor, or a G-CSF receptor deficient in amino acid residues 5 (Glu) through 195 (Leu) and amino acid residues 725 through 756 of wild-type murine granulocyte colony stimulating factor receptor (see, e.g., page 9, lines 16-24, of the specification).

Applicants again direct the Office's attention to the Ueda Declaration where Dr. Ueda states (paragraph 3):

> Estrogen receptors are part of a conserved and well-characterized family of proteins. The sequences of various members of the estrogen receptor family were known at the time the application was filed. For instance, the human estrogen receptor sequence was disclosed in a 1986 publication (see Greene et al., Science 231:1150-1154, 1986; copy enclosed as Exhibit D). Given that the structure of the estrogen receptor and of its estrogen-binding domain was known at the time the application was filed, one skilled in the art would readily recognize whether a given sequence is that of an estrogen

receptor. Moreover, a skilled artisan, at the time of filing, would have recognized an estrogen-binding domain of an estrogen receptor.

In sum, Applicants submit that the specification provides adequate written description of the fusion proteins encompassed by the present claims.

CONCLUSION

Applicants submit that the application is now in condition for allowance, and this action is hereby respectfully requested. Nonetheless, if there are any remaining issues, Applicants respectfully request a teleconference with the Examiner to bring this case into condition for allowance.

Enclosed is a Petition to extend the period for submitting an Appeal Brief pursuant to the Notice of Appeal filed on June 5, 2006 for five (5) months, to and including January 5, 2007, and a check in payment of the required extension fee.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 5 January 2007

James D. DeCamp, Ph.D.
Reg. No. 43,580

JAN M. TITTER, Ph.D.
Reg. No. 52,290

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045